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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/133,766	08/12/98	HELM B	HELM-ET-ALPC

HM12/0518

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EXAMINER	
SCHWADRON, R	
ART UNIT	**PAPER NUMBER**
1644	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/133,766	Applicant(s) Helm et al.
	Examiner Ron Schwadron, Ph.D.	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Mar 12, 1999* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *16-24* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *16-24* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

15. Claims 16-24 are under consideration. Claims 16-18,20,24 have been amended.

RESPONSE TO APPLICANTS ARGUMENTS

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claim 19 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

It is apparent that the RBL-2H3 cell line is required to practice the instant invention as cited in the claims. As a required element, the RBL-2H3 cell line must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If said cell line is not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the instant cell line. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the RBL-2H3 line. There is no indication that the RBL-2H3 cell line was publicly available and there is inadequate guidance in the specification as to how the RBL-2H3 cell line was produced. In addition, the identifying information set forth in 37 CFR 1.809 (d) should be added to the specification. See 37 CFR 1.801-1.809 for additional explanation of these requirements. The requirements under 37 CFR 1.808 can be met by submission of an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by

an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability of the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

Regarding applicants comments in page 3 of the instant amendment, applicant has not complied with 37 CFR 1.808. The requirements under 37 CFR 1.808 can be met by submission of an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability of the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

18. Regarding priority with regards to the application of prior art, there is no disclosure of the inventions of claims 17,18 in foreign priority document GB 9224956.4. Regarding claims 17 and 18, there is no disclosure in foreign priority document GB 9224956.4 of the method of claim 17 using "cell line of mast cell or basophil liniage and is transfected with a moiety capable of binding human IgE" or using a "high-secretor variant". Foreign priority document GB 9224956.4 does disclose the method of claim 19.

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having
> ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claim 17 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (J. Clin. Immunoassay) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Wilson et al. teach the RBL-2H3 cell line transfected with the α chain of the human FcεR1 (see Table 1), which is a "secretor variant" of untransfected RBL-2H3 cell line, in that the untransfected RBL-2H3 does not respond in a secretory manner to human IgE (see page 91, column 2, last paragraph). Wilson et al. teach a test allergen (eg. see Figures 1-3). Wilson et al. teach a means to determine the absence or presence of an immune response (see abstract). Wilson et al. teach the use of a radioactive marker (eg. tritiated 5HT) to measure the immune response of allergen challenged IgE sensitized RBL-2H3 cell line transfected with the α chain of the human FcεR1. Wilson et al. do not teach the claimed method. Wilson et al. teach that "following sensitization with hIgE or anti-hFcεR1α antibody, transfected clones support the release of mast cell mediators such as 5-hydroxytryptamine and histamine upon challenge with antigen or cross linking antibody."(page 240, column 2). A routineer would have used the aforementioned method to screen for allergenicity of a substance because Wilson et al. teach that sensitized transfected clones support the release of mast cell mediators such as 5-hydroxytryptamine and histamine upon challenge with allergen antigen. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Wilson et al. teach the RBL-2H3 cell line transfected with the α chain of the human FcεR1 (see Table 1), which is a "secretor variant" of untransfected RBL-2H3 cell and the use of said cell line to study allergic sensitization and a routineer would have used the aforementioned method to screen for allergenicity of a substance because Wilson et al. teach that sensitized transfected clones support the release of mast cell mediators such as 5-hydroxytryptamine and histamine upon challenge with allergen antigen. One of ordinary skill in the art would have been motivated to do the aforementioned because Wilson et al. teach that "following sensitization with hIgE or anti-hFcεR1α antibody, transfected clones support the release of mast cell mediators such as 5-hydroxytryptamine and histamine upon challenge with antigen or cross linking antibody."(page 240, column 2).

Regarding applicants arguments, there is no disclosure of the inventions of claims 17,18 in foreign priority document GB 9224956.4. Regarding claims 17 and 18, there is no disclosure in foreign priority document GB 9224956.4 of the method of claim 17 using "cell line of mast cell or basophil liniage and is transfected with a moiety capable of binding human IgE" or using a "high-secretor variant".

21. Claims 16-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al. (US Patent 4,559,310) in view of Gilfillan et al. and Levi-Schaffer et al. for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Cantor et al. teach methods for the determining the allergic status of an individual that utilize mast cell lines. Cantor et al. teach that mediators are released by mast cells after sensitization to an allergen and exposure to an allergen (see Abstract). Cantor et al, do not teach that the mast cell line is a "secretor variant". Cantor et al. teach that the response of the mast cell can be measured by assaying the release of secreted mediators such as histamine, which are measured using immunoassays including radioimmunoassays (eg. which would utilize radiolabelled histamine, see column 9). A routineer would have used any art known immunoassay (eg. ELISA using chromogen) to measure the release of mast cell mediators. A routineer would measured any mediator which the art recognized as being produced by mast cells such as arachadonic acid. Gilfillan et al. teach the RBL-2H3 cell line transfected with the α chain of the human FcεR1 (see Table 1), which is a "secretor variant" of untransfected RBL-2H3 cell line, in that the untransfected RBL-2H3 does not respond in a secretory manner to human IgE (see page 91, column 2, last paragraph). Gilfillan et al. teach that RBL-2H3 cell line transfected with the α chain of the human FcεR1 can be sensitized via exposure to human IgE (see page 2447, column 2). Gilfillan et al. teach that RBL-2H3 cell line transfected with the α chain of the human FcεR1 mediates all of the signal transduction events mediated by the untransfected RBL-2H3 cell when the untransfected cell line is exposed to rat IgE. Thus, Gilfillan et al. establish that the RBL-2H3 cell line transfected with the α chain of the human FcεR1 is functionally active with regards to the ability of said cell line to mediate human IgE/human FcεR1 interaction mediated responses. Cantor et al. teach the desirability of using mast cells derived from the species to be tested in assays for determining allergic sensitivity. A routineer would have used the RBL-2H3 cell line transfected with the α chain of the human FcεR1 in the methods taught by Cantor et al. as a convenient source of human IgE reactive mast cells. Levi-Schaffer et al. teach that mast cells activation results in the release of mediators that cause the signs and symptoms of the allergic response (see page 308). Levi-Schaffer et al. teach that mast cells respond to IgE dependent or IgE-independent activators (see page 308)). A routineer would have used the aforementioned methods in the absence of a sensitizing agent to screen for allergenicity of a substance because

Levi-Schaffer et al. teach that mast cell activation results in the release of mediators that cause the signs and symptoms of the allergic response (see page 308) and that mast cells respond to IgE-independent activators . It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the instant inventions because Cantor et al. teach methods for the determining the allergic status of an individual that utilize mast cell lines, while Gilfillan et al. teach that RBL-2H3 cell line transfected with the α chain of the human FcεR1 can be sensitized via exposure to human IgE (see page 2447, column 2) and Levi-Schaffer et al. teach that mast cell activation results in the release of mediators that cause the signs and symptoms of the allergic response (see page 308) and that mast cells respond to IgE dependent or IgE-independent activators. One of ordinary skill in the art would have been motivated to do the aforementioned because Levi-Schaffer et al. teach that mast cell activation results in the release of mediators that cause the signs and symptoms of the allergic response, thus indicating that the antigen which causes mast cell activation is an allergen and because Levi-Schaffer et al. teach that mast cells respond to IgE dependent or IgE-independent activators.

Regarding applicants comments, Levi-Schaffer et al. teach that mast cell activation results in the release of mediators that cause the signs and symptoms of the allergic response (see page 308). Levi-Schaffer et al. teach that mast cells respond to IgE dependent or IgE-independent activators (see page 308)). A routineer would have used the methods disclosed in the instant rejection in the absence of a sensitizing agent to screen for allergenicity of a substance because Levi-Schaffer et al. teach that mast cell activation results in the release of mediators that cause the signs and symptoms of the allergic response (see page 308) and that mast cells respond to IgE-independent activators. Regarding applicants comments that IgE independent inactivation is mediated via FcεR1, there is no evidence of record that IgE independent inactivation is mediated via FcεR1. A routineer would have used any mast cell in the claimed method (including those recited in the claims and rendered obvious in the instant rejection) because Levi-Schaffer et al. teach that mast cells respond to IgE dependent or IgE-independent activators (see page 308)). A routineer would have used the methods disclosed in the instant rejection in the absence of a sensitizing agent to screen for allergenicity of a substance because Levi-Schaffer et al. teach that mast cell activation results in the release of mediators that cause the signs and symptoms of the allergic response (see page 308) and that mast cells respond to IgE-independent activators.

22. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the claimed invention which recites "which when exposed to a preselected substance results in at least 25-45% mediator release". Regarding applicants comments about the specification, page 12, "25-45% mediator release" is disclosed in said passage of the specification as a definition for Table 2 wherein it refers to specific experiments performed using RBL-2H3 wherein specific mediators were released. It is not defined as a definition of "high secretor" or used in the context of any mediator or used in the context of cells other than RBL-2H3. There is no written description of the scope of the claimed invention in the specification as originally filed (the claimed invention constitutes new matter).

23. No claim is allowed.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-

3014.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644
May 17, 1999